6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, and/or measuring, and/or monitoring xylene, its metabolites, and other biomarkers of exposure and effect to xylene. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH).

Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

The analytical methods used to quantify xylene in biological and environmental samples are summarized below. Table 6-l lists the applicable analytical methods used for determining xylene in biological fluids and tissues. Table 6-2 lists the methods used for determining xylene in environmental samples.

6.1 BIOLOGICAL MATERIALS

Extensive commercial, industrial, and domestic use of volatile organic chemicals such as xylene virtually assures that the general population will be exposed to this class of chemicals to some extent. The determination of trace amounts of xylene in biological tissues and fluids has been restricted to only a limited number of analytical methods. These include gas chromatography coupled with mass spectrometry (GC/MS), gas chromatography coupled with hydrogen flame ionization detection (GC/PID), and high-performance liquid chromatography (HPLC).

Xylene can be detected at parts-per-trillion (ppt) levels in whole human blood using a purge and trap apparatus followed by GC/MS; however, this method does not distinguish between *m*- and *p*-xylene (Ashley et al. 1992). Antifoam agents are frequently used, although a method has been developed that does not require this additive (Cramer et al. 1988). The use of a dynamic headspace purge at room temperature reduces the absolute recoveries of the late eluting compounds. An advantage of this

TABLE 6-1. Analytical Methods for Determining Xylene in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Human blood	Adsorb directly to Amberlite XAD-2 resin; extract with carbon disulfide	GC/FID	No data	77–98 (*m*-xylene)	Norstrom and Scheepers 1990
Human blood	Purge and trap sample on Tenax TA trap	GC/MS	1 ng/mL (*m*-xylene)	No data	Cramer et al. 1988
Human blood	Purge and trap sample on sorbent	GC/MS	5.2 ng/mL	No data	Antoine et al. 1986
			0.019 ng/mL (*m*-, *p*-xylene); 0.035 ng/mL (*o*-xylene)	No data	Ashley et al. 1992
Tissues and body fluids	Saturate sample with sodium chloride and seal in a vial; inject into gas chromatograph	GC/FID and GC/MS	0.05 mg/100 g (*m*-, *p*-xylene); 0.01 mg/100 g (*o*-xylene)	No data	Bellanca et al. 1982
Urine	Derivatize or methylate sample with HCl and methanol; cool; extract with chloroform	GC/FID	<0.25 g/L	110.7 (*m*-MHA)	de Carvalho et al. 1991

TABLE 6-1. Analytical Methods for Determining Xylene in Biological Materials (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	Extract sample with THA-OH; alkylate with isopropyl bromide; wash with silver sulfate; dry; redissolve in ethyl acetate	GC/FID	1 ng (*o*-, *p*-, *m*-MHA)	94.2 (*o*-MHA); 96.0 (*m*-MHA); 97.6 (*p*-MHA)	Kataoka et al. 1991
Urine	Adsorb to filter paper; extract with methanol; dilute with mobile phase or water	HPLC	4 ng (*o*-MHA and *m*-MHA)	99–99.9 (*o*-MHA); 97.2–99.9 (*m*-MHA)	Astier 1992
Urine	Adsorb to Sep-Pack C_{18} cartridge; elute with methanol	HPLC	10 µg/mL (xyl-*m*)	94.7–96.1 (xyl-*m*)	Tanaka et al. 1990
Urine	Acidify with H_2SO_4; extract with methyl-*t*-butyl ether; concentrate	HPLC	0.1 µmol (*o*-, *p*-, *m*-MHA)	91 (*o*-MHA); 107 (*m*-MHA); 113 (*p*-MHA)	Tardif et al. 1989
Urine	Acidify with HCl, saturate with sodium chloride; extract with ethyl acetate; dry and redissolve in distilled water	HPLC/ UV	0.2 mg/mL (methyl hippuric acid; method does not distinguish between *p*- and *m*-isomers)	98	NIOSH 1994 (Method 8301)

TABLE 6-1. Analytical Methods for Determining Xylene in Biological Materials (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	Acidify sample and extract with ethyl acetate and methylating solution	GC/FID	5 mg/L	81.5 (*o*-MHA); 82.2 (*m*-MHA); 84.8 (*p*-MHA)	Caperos and Fernandez 1977
Urine	Adjust pH of sample to 2.0; extract with ethyl-acetate	GC/FID	No data	98 (*m*-MHA)	Engstrom et al. 1976
Urine	Acidify sample with HCl and extract with ethylacetate; add methanol to ethylacetate extract; methylate extract with diazomethane in diethyl ether solution	GC/FID	No data	88.7–95 (*m*-MHA); 79.3–82 (*p*-MHA)	Morin et al. 1981
Urine	Acidify sample	HPLC	No data	CV = 4.8	Astier 1992
Urine	Acidify sample with HCl; extract with *n*-butyl chloride:iso-propanol (9:1)	HPLC	0.1 mg/mL (*m*-MHA)	No data	Poggi et al. 1982

TABLE 6-1. Analytical Methods for Determining Xylene in Biological Materials (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	Adjust pH of sample to 2.0; extract with methyl ethyl ketone; add phenacyl bromide solution to extract and heat	HPLC	0.02 µg/sample (*m*-MHA); 0.02 µg/sample (*p*-MHA)	No data No data	Sugihara and Ogata 1978
Urine	Add sample specimen to methanol; centrifuge	HPLC	6 mg/L (*o*-MHA); 8 mg/L (*m*-MHA); 8 mg/L (*p*-MHA)	102 (*o*-MHA); 102.4 (*m*-MHA); 99.5 (*p*-MHA)	Ogata and Taguchi 1987
Urine	Acidify sample; extract with chloroform and concentrate	TLC	6 µg/mL (*m*-MHA)	100 (*m*-MHA)	Bieniek and Wilczok 1981
Exhaled breath	Trap sample on charcoal cloth; desorb with carbon disulfide	GC/FID	0.06 ppm (*m*-xylene)	90	Glaser and Arnold 1989; Glaser et al. 1990
Exhaled breath	Sorb to Tenax TA tube; thermally purge	GC/FID	0.03 ppm	60 (*m*-xylene)	Glaser et al. 1990

TABLE 6-1. Analytical Methods for Determining Xylene in Biological Materials (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Exhaled breath	Sorb to Tenax GC tube; dry; thermally desorb	GC/MS	0.50 µg/m^3	No data	Pellizzari et al. 1988
Whole body (mice)	Kill mice and inject with solvent sample; homogenize sample in liquid nitrogen; evaporate liquid nitrogen and extract with carbon disulfide	GC/FID	No data	86 (*m*-xylene)	Tsuruta and Iwasaki 1984
Fish	Freeze sample; homogenize in liquid nitrogen; vacuum distillation	GC/MS equipped with fused-silica capillary column	No data	No data	Hiatt 1983

CV = coefficient of variation; GC/FID = gas chromatography/flame ionization detector; GC/MS = gas chromatography/mass spectrometry; HCl = hydrochloric acid; HPLC = high performance liquid chromatography; H_2SO_4 = sulfuric acid; MHA = methylhippuric acid; THA-OH = tetrahexyl ammonium hydroxide; TLC = thin-layer chromatography; UV = ultra violet; xyl-*m* = *N*-acetyl-*s*-xylyl-L-cysteine

GC/MS technique is that it can be used in conjunction with selected ion monitoring to obtain better sensitivity of target compounds (such as National Priority List Pollutants) at ppt levels (Cramer et al. 1988).

To overcome the low recoveries obtained with the purge and trap method, another extraction procedure is recommended that uses Amberlite XAD-2 adsorbent resin present in the blood collection tube when the sampling takes place. This method dispenses with the readsorption of the hydrocarbon from the sampling tube to the polymer and gives recoveries of 77-98% (Norstrom and Scheepers 1990).

The use of GC/FID followed by a combination of packed and open tubular capillary GC and GC/MS to detect and quantify the isomers of xylene in human tissues and fluids has been reported in the literature. Brain, liver, lung, kidney, and blood samples of individuals who died following occupational exposure to several organic solvents were analyzed using a combination of capillary columns (Bellanca et al. 1982). The sensitivity and resolution of the isomers of xylene were increased, and detection limits of 0.05 mg, 0.05 mg, and 0.01 mg per 100 grams of sample were obtained for *m*-, *o*-, and *p*-xylene, respectively (Bellanca et al. 1982). Despite this increased resolving power, adequate separation of *m*-xylene and *p*-xylene was unattainable.

Exposure to xylene may also be indicated by its presence in exhaled breath. Xylene in mainstream breath may be determined by exhaling through a charcoal cloth (Glaser and Arnold 1989); xylene in sidestream breath is trapped using a two-stage Tenax TA sorbent sampler (Glaser et al. 1990) or a Tenax GC cartridge (Pellizzari et al. 1988). The Tenax cartridge is dried over calcium sulfate, and then the xylene is thermally desorbed for GC/MS. Correlations with carbon dioxide measurements were 90% and 60% for mainstream and sidestream breath, respectively (Glaser et al. 1990), with a quantification limit of 0.4 µg/L of *m*-xylene for a 50-L sample (Glaser and Arnold 1989). The detection limit (LOD) was 0.50 µg/m^3 with a quantification limit five times the LOD for a 15-L breath sample (Pellizzari et al. 1988).

In addition to direct measurement of xylene in biological tissues and fluids, it is also possible to determine the concentration of its metabolites in biological fluids. A simple, sensitive, and specific automated HPLC technique was developed for direct and simultaneous quantification of *o*-, *m*-, and *p*-methylhippuric acids, the metabolites of *o*-, *m*-, and *p*-xylene, respectively (Ogata and Taguchi 1987; Sugihara and Ogata 1978; Tardif et al. 1989). A possible disadvantage of the HPLC technique is that

at low concentrations (less than 0.6 mg/L) in urine, these methylhippuric acids may not be distinguishable from similar compounds. However, addition of a mobile phase, consisting of mixture of acetonitrile and 1% phosphoric acid, has been used to distinguish between xylene metabolites and other solvents such as benzene and toluene in the urine (Astier 1992). Use of methanol as a solvent for the urine obviates the need for the customary ethylether extraction step and allows direct urine injection for HPLC (Ogata and Taguchi 1988). *N*-acetyl-*S*-xylyl-L-cysteine, a mercapturic acid, is also a urinary metabolite of xylene that may be detected by direct HPLC (Tanaka et al. 1990). The HPLC method recommended by NIOSH (1994) does not distinguish between *p*- and m-methyl hippuric acids.

Other techniques that have been successful in quantitatively determining urinary concentrations of metabolites of xylene include GC/FID, GC/MS, and thin layer chromatography (TLC). GC/FID and GC/MS offer the possibility of excellent analytical sensitivity and specificity for urinary metabolites of xylene (Caperos and Femandez 1977; de Carvalho et al. 1991; Engstrom et al. 1976; Kataoka et al. 1991; Kira 1977; Morin et al. 1981; Poggi et al. 1982). However, most GC analytical methods require the urinary metabolites to be chemically transformed into methyl esters or trimethyl silyl derivatives using ethylacetate or diazomethane. This transformation, however, is problematic and may subsequently cause low reproducibility (Caperos and Femandez 1977; Engstrom et al. 1976; Morin et al. 1981; Poggi et al. 1982). The methylhippuric acid metabolites of the xylene isomers may be distinguished using an extractive alkylation procedure followed by capillary CC analysis (Kataoka et al. 1991). An extraction method using less toxic reagents (hydrochloric acid with methanol) has been developed (de Carvalho et al. 1991).

A simple and highly reproducible TLC method has been developed for the detection and separation of *m*- or *p*-methylhippuric acid in the urine of individuals exposed to a mixture of volatile organic solvents (Bieniek and Wilczok 1981). However, the authors noted that this analytical technique is time consuming. Furthermore, the developing agent used in this technique (*p*-dimethylamine benzaldehyde in acetic acid) has the disadvantage that it is irritating to the eyes and mucous membranes.

When measuring hippuric acids in the urine of workers exposed to xylenes, NIOSH (1994) recommends that a complete spot voiding sample be collected at the end of the shift after 2 days of exposure. As a preservative, a few crystals of thymol should be added to the sample. It should be

stored at 4°C if analysis is within 1 week. The sample should remain stable for 2 months if it is stored at -20°C.

6.2 ENVIRONMENTAL SAMPLES

A gas chromatograph equipped with an appropriate detector is the basic analytical instrument used for determining environmental levels of xylene. Precautions in the isolation, collection, and storage of xylene in environmental media are necessary to prevent loss of the volatile xylene compounds to the air.

The most common method for detecting aromatic hydrocarbons in air is the adsorption of the vapors to either activated charcoal with extraction using carbon disulfide or adsorption to a polymer adsorbent, such as Tenax GC, with thermal desorption. Each method is then followed by injection of the desorbed sample into a gas chromatograph equipped with FID (Brown 1988a, 1988b; NIOSH 1994). The activated charcoal method requires a 12-L air sample, while the polymer adsorbent uses a smaller 5-L sample for determination of the xylene in the sub-parts-per-million range. A GC/MS method has also been developed which uses an adsorbent tube with layers of Tenax, Amberlite, and charcoal (Chan et al. 1990). The use of a molecular sieve to remove water vapor prior to adsorption has been recommended to increase recovery of the hydrocarbons (Whitman and Johnston 1964). A computer-controlled, high-speed GC system has been developed for rapid analysis of volatiles in air (and other media with appropriate vapor generation). The system combines an electrically heated cold-trap inlet (with a vacuum backflushing device on the GC) with a convention FID. The advantage of the system is that a complete analysis cycle requires only 10 seconds to detect *p*-xylene at a level of 13.4 ppb (Rankin and Sacks 1991).

A differential optical absorption spectrophotometer has also been used to monitor *o*-xylene in air; this method gives a correlation coefficient of approximately 0.66 when compared with standard GC methods (Stevens and Vossler 1991).

An automated gas chromatograph with photoionization detector (GC/PID) has been developed by Hester and Meyer (1979) to identify gas-phase hydrocarbons (including xylene) for complex systems such as vehicle exhaust gas. The GC/PID method allows for measurement of sub-parts-per-billion level concentrations of air contaminants and does not require trapping or freeze-concentration of

TABLE 6-2. Analytical Methods for Determining Xylene in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Collect sample on porous polymer adsorbent; thermally desorb	GC/FID	0.1 ppm	No data	Brown 1988b
Air	Sorption to a tube containing Tenax, Ambersorb XE-340, and charcoal; thermally desorb	GC/MS	4.0 ng/tube (5–50-L air sample)	93–103 (*o*-xylene); 90.8 (*p*-, *m*-xylene)	Chan et al. 1990
Air	Draw sample through copper tubing with a diaphragm pump	GC/PID	0.3 ppb	No data	Hester and Meyer 1979
Air	Absorption on Tenax GC air sampler	GC/MS	No data	No data	Hampton et al. 1982
Air	Collect on coconut shell charcoal personal sampler; desorb with carbon disulfide	GC/FID	2.6 mg	No data	NIOSH 1994 (Method 1501)
Air	Pump air sample through charcoal tubes; extract charcoal with carbon disulfide	GC/FID	<0.05 ppm (*o*-xylene); <0.05 ppm (*p*-xylene)	51–86 (*o*-xylene); 51–86 (*p*-xylene)	Brown 1988a; Otson et al. 1983

TABLE 6-2. Analytical Methods for Determining Xylene in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Collect sample in Tedlar bags by means of an automated sequential large air sampler	GC/FID	No data	No data	Lonneman et al. 1974
Air	Collect air on activated charcoal; desorb with carbon disulfide; shake with 75% H_2SO_4	GC/FID	1 µg/µL	92–100	Esposito and Jacobs 1977
		LC/UV	No data	92–104	
Air	Collect sample in pressurized stainless steel cannister	GC-FID/PID	1.3 pg/sample (*o*-xylene)	No data	Nutmagul et al. 1983
Air	Collect sample in a pressurized cannister	GC-FID/ECD and GC/MS	<1 ppm	No data	Pleil et al. 1988
Air	Collect sample on silica gel; extract with isopropyl benzene	GC	No data	>99%	Whitman and Johnston 1964
Drinking water	Purge and trap on sorbent	GC/FID	<1 µg/L (*o*-xylene); <1 µg/L (*m*-xylene)	75 (*o*-xylene); 87 (*m*-xylene)	Otson and Williams 1982

TABLE 6-2. Analytical Methods for Determining Xylene in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Drinking water	Extract sample in hexane	GC/FID	2 µg/L (*o*-xylene); 2 µg/L (*m*-xylene); 2 µg/L (*p*-xylene)	80–96 (*o*-xylene); 80–83 (*m*-xylene); 78–85 (*p*-xylene)	Otson and Williams 1981
Water	Purge and trap; methyl-silicone-coated packing is recommended; desorb thermally	GC-PC/MS	0.1–0.5 µg/L	No data	APHA 1992 (equivalent to EPA Method 524)
Water	Purge and trap; methyl-silicone-coated packing is recommended; desorb thermally	GC-CC/MS	0.1–0.5 µg/L	Wide-bore column 103 (*o*-xylene) 97 (*m*-xylene) 104 (*p*-xylene) Narrow-bore column 106 (*o*-xylene) 106 (*m*-xylene) 97 (*p*-xylene)	APHA 1992 (equivalent to EPA Method 524)

TABLE 6-2. Analytical Methods for Determining Xylene in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Groundwater	Solid-phase microextration (methyl-silicone fiber coated with methyl-silicone film)	GC/FID	1 µg/L	No data	Arthur et al. 1992
Water	Purge and trap; methyl-silicone-coated packing is recommended; desorb thermally	GC-PC/PID	0.01–0.05 µg/L	90 (*o*-xylene) 90 (*m*-xylene) 85 (*p*-xylene)	APHA 1992 (equivalent to EPA Method 503.1)
Water	Purge and trap; methyl-silicone-coated packing is recommended; desorb thermally	GC-CC/PID	No data	90 (*o*-xylene) 100 (*m*-xylene) 99 (*p*-xylene)	APHA 1992 (equivalent to EPA Method 502.2)
Soil	Extract sample with methanol; centrifuge	GC	No data	No data	Anderson et al. 1991
Sediment (clay)	Shake sample with water; purge and trap on Porapak N cartridges; elute with MeOH	GC-ECD/PID	7 ng/g	70–77 (*p*-xylene); 68–79 (*o*-xylene)	Amin and Narang 1985
		GC/ECD	1 ng/g	No data	

TABLE 6-2. Analytical Methods for Determining Xylene in Environmental Samples (*continued*)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Waste	Extract waste with hexane	GC/MS	No data	No data	Austern et al. 1975
Waste	Add sample to a small volume of ethanol and dilute with water or raw wastewater; adjust the pH; extract with Freon-TF	GC/FID	No data	No data	Austern et al. 1975

CC = capillary column; ECD = electron capture detector; FID = flame ionization detector; GC = gas chromatography; H_2SO_4 = sulfuric acid; MeOH = methanol; MS = mass spectrometry; LC = liquid chromatography; PC = packed column; PID = photoionization detector; UV = ultraviolet spectrometry

samples before analysis. These latter preconcentration steps are usually necessary because of the limited sensitivity of FID techniques commonly used in the analysis of environmental samples. A limitation of the GC/PID technique is that *m-* and *p*-xylene are detected but not well separated. GC/PID in tandem with FID was used to obtain a more sensitive method to determine xylene levels in the air. A detection limit of $1.3x10^{-12}$ g of *o*-xylene per sample was achieved (Nutmagul et al. 1983).

A purge and trap gas chromatographic method involving photoionization detection has been developed by EPA to analyze volatiles in water (APHA 1992). A confirmatory analysis by a second analytical column or by GC/MS is advised by EPA. The purge and trap gas chromatographic method can detect the isomers of xylene and has a detection limit for *o*-, *m-,* and *p*-xylene of 0.2 ppb (Otson and Williams 1981, 1982; Saunders et al. 1975). A purge and trap method using GC/MS has also been used to detect xylene in waste water (Koe and Tan 1990).

Emissions of volatile organic compounds from surface waters, including ponds at hazardous waste treatment facilities, may be directly measured by the use of enclosure methods (such as a flux chamber or surface impoundment simulator connected to collection canisters) followed by GC/FID with an electron capture detector. Emission rates of 0.5 mg/minute/m' could be measured using the surface impoundment simulator with a precision of 3% relative standard deviation (Gholson et al. 1991).

GC using both electron capture detection (ECD) and photoionization detection (PID) has been employed to determine xylene levels in sediment samples (Amin and Narang 1985). The authors indicated that their method involved transfer of samples between containers, and a considerable loss of volatile compounds was obtained.

A procedure has been developed to characterize volatile xylene compounds from fish samples by GC/MS using a fused-silica capillary column (FSCC) and vacuum distillation (Hiatt 1983). The FSCC provides a more attractive approach than packed columns for chromatographic analysis of volatile aromatic organic compounds. An FSCC can be heated to a higher temperature (350°C) than that recommended for packed column, thereby improving the resolution (in ppb levels) of compounds and reducing column retention times. A physical limitation for compounds that can be detected, however, is that the vapor pressure of the compound must be greater than 0.78 torr (≈50ºC) in the sample chamber (Hiatt 1983).

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of xylene is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of xylene.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. The methods for determining xylene levels in blood and tissue samples and exhaled breath, GC/MS or GC/FID, have sufficient sensitivity to measure xylene levels associated with background levels of exposure as well as xylene levels at which biological effects occur. GC/MS has been employed to detect *o*-xylene at ppm levels in the blood (Ashley et al. 1992; Cramer et al. 1988). However, development of a GC/MS method that incorporates a less rigorously heated purge would be useful. Heated purges currently used in GC/MS have the disadvantage of reducing the absolute recoveries of volatile organic solvents. Better resolution and sensitivity are achievable with the application of a capillary GC/MS column and selection of an appropriate detector or detector combination as an alternative to the packed column approach currently in use. Also, there is a growing need for analytical methods to efficiently separate and quantify trace levels of the isomers of xylene in biological media.

Analytical methods are also available to detect and quantify the xylene metabolites present in the urine which have been correlated with exposure levels (Kawai et al. 1991; Ogata et al. 1979). These methods, HPLC (Astier 1992) and GC (coupled with MS or FID) (de Carvalho et al. 1991; Kataoka et al. 1991; -Poggi et al. 1982), have been well characterized with respect to their precision, accuracy,

reliability, and specificity and have sufficient sensitivity to measure xylene metabolite levels associated with biological effects. However, these methods may not be sensitive enough to measure metabolite levels associated with background exposure levels.

Currently, no methods are available to quantitatively correlate monitored levels of xylene in tissues with exposure levels or toxic effects in humans, although simultaneous measurement of xylene in exhaled breath and ambient air may prove instrumental in indicating exposure, particularly in the workplace (Glaser et al. 1990). These methods would provide the ability to evaluate possible health effects in humans resulting from exposure to xylene.

No specific biomarkers of effect have been clearly associated with xylene exposure. Some biological parameters such as hepatic microsomal enzyme activities and central nervous system activity (measured by evoked potentials or tests of memory and reaction time) have been tentatively linked with xylene exposure, but insufficient data exist to adequately assess the analytical methods associated with measurement of these potential biomarkers.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Methods for determining xylene and its degradation products in environmental media are necessary to identify contaminated areas and to determine whether the levels at contaminated sites constitute a concern for human health. Standardized methods are available to detect xylene in air (Brown 1988a, 1988b; Chan et al. 1990; Rankin and Sacks 1991), waste water (Koe and Tan 1990), drinking water (EPA 1981a; Otson and Williams 1981, 1982), fish (Hiatt 1983), and clay sediments (Amin and Narang 1985). There is growing need for simultaneously achieving lower (< ppb) detection limits, separating the m- and *p*-isomers of xylene, and obtaining an adequate sample recovery. Such methods would provide useful information for assessing the biological effects of exposure to xylene and for delineating dose-response relationships. A combination of capillary gas chromatography coupled to a multi-detector system, nuclear magnetic resonance (NMR) spectroscopy, and infra-red (IR) spectroscopy would be useful for the accurate identification and measurement of the isomers of xylene in complex environmental systems.

6.3.2 On-going Studies

R.E. Letz of the Mount Sinai School of Medicine in New York is estimating the central nervous system concentrations of various solvents (including xylene) in industrial spray painters. This investigator proposes using industrial hygiene sampling and exhaled breath and urine analyses coupled with mathematical dose models to estimate these concentrations.

No other on-going studies concerning the identification of xylene in biological materials or environmental samples were identified.